

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Ms. Catherine M. McCarty on 8-7-06.

The application has been amended as follows:

Claim 1: The last line, delete the sentence: **“when A represents thiophene, then R¹ is not 4-pyridinyl or 3-pyrazolyl.”** This is an extraneous proviso.

Claim 21: The first two lines, delete **“or a disease with an inflammatory component”**, and insert the phrase – selecting from the group consisting of asthma, rheumatoid arthritis, multiple sclerosis, chronic obstructive pulmonary disease, and rhinitis – in its place.

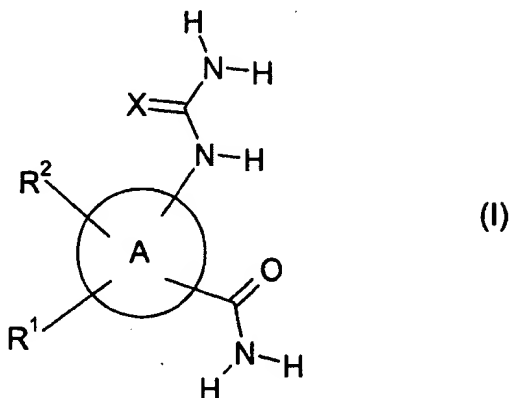
Cancel claims 20, 22-25 and 29.

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Previously presented) A compound of formula (I)



A represents thiophene;

R^1 represents a phenyl group; said phenyl being optionally substituted by one or more substituents selected independently from halogen, cyano, nitro, $-NR^3R^4$, $-CONR^5R^6$, $-COOR^7$, $-NR^8COR^9$, $-SR^{10}$, $-S(O)_mR^{10}$, $-S(O)_2NR^5R^6$, $-NR^8SO_2R^{10}$, C_1 - C_6 alkyl, trifluoromethyl, $-(CH_2)_nR^{11}$, $-O(CH_2)_nR^{11}$ or $-OR^{12}$;

R^2 represents hydrogen, halogen, cyano, nitro, $-NR^{13}R^{14}$, $-CONR^{15}R^{16}$, $-COOR^{17}$, $-NR^{18}COR^{19}$, $-S(O)_mR^{20}$, $-S(O)_2NR^{15}R^{16}$, $-NR^{18}SO_2R^{20}$, C_1 - C_2 alkyl, trifluoromethyl, C_2 - C_3 alkenyl, C_2 - C_3 alkynyl, trifluoromethoxy, C_1 - C_2 alkoxy or C_1 - C_2 alkanoyl;

X represents oxygen or sulfur;

each of $R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}$ and R^{12} independently represent a hydrogen atom or C_1-C_6 alkyl;

R^{11} represents $NR^{21}R^{22}$ where R^{21} and R^{22} are independently hydrogen or C_1-C_6 alkyl optionally substituted by C_1-C_4 alkoxy; or R^{21} and R^{22} together with the nitrogen atom to which they are attached form a 5- or 6-membered saturated ring optionally containing a further O, S or NR^{23} group where R^{23} is hydrogen or C_1-C_6 alkyl; or R^{11} represents OR^{24} where R^{24} represents C_1-C_6 alkyl;

each of $R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}$ and R^{20} independently represent a hydrogen atom or C_1-C_2 alkyl;

m represents an integer 0, 1 or 2;

n represents an integer 2, 3 or 4;

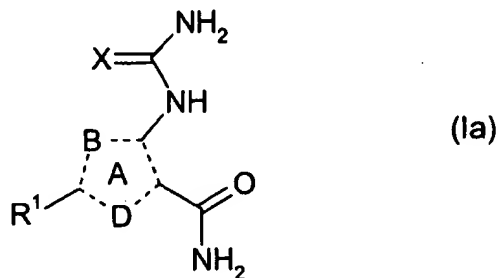
and optical isomers, racemates, and tautomers thereof and pharmaceutically acceptable salts or solvates thereof:

provided that:

~~[when A represents thiophene, then R^1 is not 4-pyridinyl or 3-pyrazolyl.]~~

2. (Original) A compound of formula (I), according to Claim 1, wherein X represents oxygen.

3. (Previously presented) A compound of formula (I), according to Claim 1, in which the group A is substituted as shown below in formula (Ia), where B and D are selected from CR^2 and S, where R^2 is as defined in Claim 1 and R^{25} is hydrogen or C_1-C_6 alkyl:



Examiner's
Smdt
8-7-06

4. (Cancelled)
5. (Cancelled)
6. (Previously presented) A compound according to claim 1 in which R^2 represents H or methyl.
7. (Original) A compound according to Claim 6 in which R^2 represents H.
8. (Original) A compound of formula (I), according to claim 1, selected from:
 - 3-[(aminocarbonyl)amino]-5-phenyl-2-thiophenecarboxamide;
 - 3-[(aminocarbonyl)amino]-5-(3-chlorophenyl)-2-thiophenecarboxamide;
 - 3-[(aminocarbonyl)amino]-5-(4-fluorophenyl)-2-thiophenecarboxamide;
 - 3-[(aminocarbonyl)amino]-5-(4-chlorophenyl)-2-thiophenecarboxamide;
 - 3-[(aminocarbonyl)amino]-5-(4-isobutylphenyl)-2-thiophenecarboxamide;
 - 3-[(aminocarbonyl)amino]-5-(4-methoxyphenyl)-2-thiophenecarboxamide;
 - 3-[(aminocarbonyl)amino]-5-(3-hydroxyphenyl)-2-thiophenecarboxamide;
 - 3-[(aminocarbonyl)amino]-5-(2-chlorophenyl)-2-thiophenecarboxamide;
 - 3-[(aminocarbonyl)amino]-5-(2-methoxyphenyl)-2-thiophenecarboxamide;
 - 3-[(aminocarbonyl)amino]-5-{2-[2-(dimethylamino)ethoxy]phenyl}-2-thiophenecarboxamide;
 - 3-[(aminocarbonyl)amino]-5-{4-[2-(dimethylamino)ethoxy]phenyl}-2-thiophenecarboxamide;
 - 3-[(aminocarbonyl)amino]-5-(3-methoxyphenyl)-2-thiophenecarboxamide;
 - 2-[(aminocarbonyl)amino]-5-phenyl-3-thiophenecarboxamide;

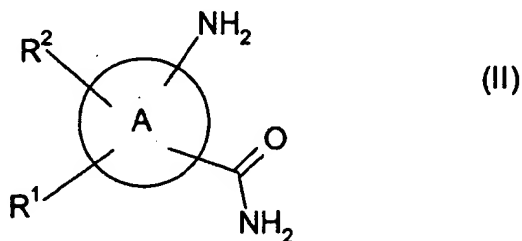
3-[(aminocarbonyl)amino]-5-{4-[2-(1-morpholinyl)ethoxy]phenyl}-2-thiophenecarboxamide;
3-[(aminocarbonyl)amino]-5-{4-[2-(1-pyrrolidinyl)ethoxy]phenyl}-2-thiophenecarboxamide;
3-[(aminocarbonyl)amino]-5-{4-[2-(1-piperidinyl)ethoxy]phenyl}-2-thiophenecarboxamide;
3-[(aminocarbonyl)amino]-5-{4-[3-(dimethylamino)propoxy]phenyl}-2-thiophenecarboxamide;
3-[(aminocarbonyl)amino]-5-{3-[2-(dimethylamino)ethoxy]phenyl}-2-thiophenecarboxamide;
3-[(aminocarbonyl)amino]-5-{3-[2-(1-morpholinyl)ethoxy]phenyl}-2-thiophenecarboxamide;
3-[(aminocarbonyl)amino]-5-{3-[2-(1-pyrrolidinyl)ethoxy]phenyl}-2-thiophenecarboxamide;
3-[(aminocarbonyl)amino]-5-{3-[2-(1-piperidinyl)ethoxy]phenyl}-2-thiophenecarboxamide;
3-[(aminocarbonyl)amino]-5-{3-[3-(dimethylamino)propoxy]phenyl}-2-thiophenecarboxamide;
3-[(aminocarbonyl)amino]-5-{2-[2-(1-morpholinyl)ethoxy]phenyl}-2-thiophenecarboxamide;
3-[(aminocarbonyl)amino]-5-{2-[2-(1-pyrrolidinyl)ethoxy]phenyl}-2-thiophenecarboxamide;
3-[(aminocarbonyl)amino]-5-{2-[2-(1-piperidinyl)ethoxy]phenyl}-2-thiophenecarboxamide;
3-[(aminocarbonyl)amino]-5-{2-[3-(dimethylamino)propoxy]phenyl}-2-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(4-chlorophenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(4-methylphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-ethyl-5-phenyl-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(4-methoxyphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(4-fluorophenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(3-fluorophenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(3-methoxyphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(3-chloro-4-methoxyphenyl)-3-thiophenecarboxamide;

2-[(aminocarbonyl)amino]-4-methyl-5-(2-chlorophenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(3-trifluoromethylphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(3-methyl-4-methoxyphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(3,5-dimethoxyphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(2,3-dimethoxyphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(4-isopropylphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(3,4,5-trimethoxyphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(3,4-dichlorophenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(4-cyanophenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(4-hydroxyphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(4-[2-(1-piperidinyloxy)]phenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(4-[2-(diethylamino)ethoxy]phenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-trifluoromethyl-5-phenyl-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-phenyl-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(4-cyanophenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(4-trifluoromethylphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(2,4-difluorophenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(4-hydroxyphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(4-chlorophenyl)-3-thiophenecarboxamide;

2-[(aminocarbonyl)amino]-5-(4-methanesulphonylphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(4-[2-(1-piperidinyl)ethoxy]phenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(4-[2-(1-(2,2,6,6-tetramethyl)piperidinyl)ethoxy]phenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(4-(thiazol-4-yl-methoxy)phenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(4-[2-(dimethylamino)ethoxy]phenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(4-[2-(diethylamino)ethoxy]phenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(4-[2-(1-morpholinyl)ethoxy]phenyl)-3-thiophenecarboxamide;
2-[(aminothiocabonyl)amino]-5-phenyl-3-thiophenecarboxamide;
and pharmaceutically acceptable salts and solvates thereof.

9. (Previously presented) A process for the preparation of a first compound of formula (I), according to claim 1, which comprises:

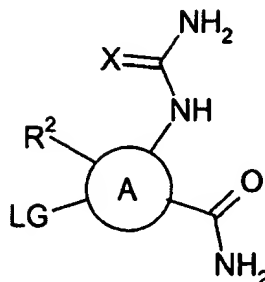
(a) reaction of a compound of formula (II):



wherein A, R¹ and R² are as defined in Claim 1, with an isocyanate (X = O) or an isothiocyanate (X = S), to produce the first compound of formula (I); or

(b) reaction of compound of formula (III) with a compound of formula (IV)

R¹-Metal



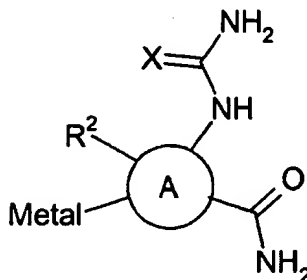
(III)

(IV)

wherein A, X, R¹ and R² are as defined in Claim 1, and LG represents a leaving group, to produce the first compound of formula (I); or

(c) reaction of compound of formula (V) with a compound of formula (VI)

R¹-LG



(V)

(VI)

wherein A, X, R¹ and R² are as defined in Claim 1, and LG represents a leaving group, to produce the first compound of formula (I).

10. (Previously presented) A pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in claim 1, in association with a pharmaceutically acceptable adjuvant, diluent or carrier.
11. (Previously presented) A process for the preparation of a pharmaceutical composition which comprises mixing a compound of formula (I), or a pharmaceutically acceptable salt or

solvate thereof, as claimed in claim 1 with a pharmaceutically acceptable adjuvant, diluent or carrier.

12-19. (Cancelled)

*Examiner's
Amend.
8-7-06*
~~20. (Previously presented) A method of treating an IKK2-mediated disease which comprises administering to a patient a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in claim 1.~~

*Examiner's
Amend.
8-7-06*
21. (Previously presented) A method of treating an inflammatory disease, ~~or a disease with an inflammatory component~~, in a patient suffering from, or at risk of, said disease, which *group consisting of asthma, rheumatoid arthritis, multiple sclerosis, chronic obstructive pulmonary disease, and rhinitis,* comprises administering to the patient a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in claim 1. *selecting from the*

~~22. (Original) A method according to claim 21, wherein the disease is asthma.~~

23. (Original) A method according to claim 21, wherein the disease is rheumatoid arthritis.

24. (Original) A method according to claim 21, wherein the disease is multiple sclerosis.

~~25. (Original) A method according to claim 21, wherein the disease is chronic obstructive pulmonary disease.~~

26. (Previously presented) A pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in claim 8, in association with a pharmaceutically acceptable adjuvant, diluent or carrier.

27. (Previously presented) A process of claim 9, further comprising converting the first compound of formula (I), or a salt thereof, into a pharmaceutically acceptable salt thereof; or converting the first compound of formula (I) into a second compound of formula (I).

28. (Previously presented) A process of claim 9, further comprising converting the first compound of formula (I) into an optical isomer thereof.

*Examiners
and
8-7-06*
~~29. (Previously presented) A method of claim 21, wherein the disease is rhinitis.~~